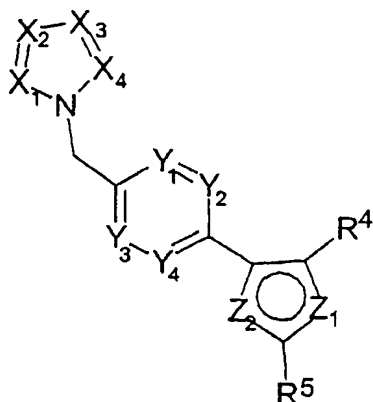


## Claims

1. A compound of formula I,



5

wherein

one of  $X_1$  and  $X_2$  represents  $-N-$  and the other represents  $-C(R^1)-$ ;

$X_3$  represents  $-N-$  or  $-C(R^2)-$ ;

- 10  $X_4$  represents  $-N-$  or  $-C(R^3)-$ ;

$R^1$ ,  $R^2$  and  $R^3$  independently represent H,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkoxy- $C_{1-6}$ -alkyl or halo;

provided that, when  $X_1$  represents  $-C(R^1)-$ ,  $X_3$  represents  $-C(R^2)-$  and  $X_4$  represents  $-C(R^3)-$ , then  $R^1$  represents H;

- 15  $Y_1$ ,  $Y_2$ ,  $Y_3$  and  $Y_4$  independently represent  $-CH-$  or  $-CF-$ ;

$Z_1$  represents  $-CH-$ ,  $-O-$ ,  $-S-$ ,  $-N-$  or  $-CH=CH-$ ;

$Z_2$  represents  $-CH-$ ,  $-O-$ ,  $-S-$  or  $-N-$ ;

provided that:

- (a)  $Z_1$  and  $Z_2$  are not the same;
- 20 (b) when  $Z_1$  represents  $-CH=CH-$ , then  $Z_2$  may only represent  $-CH-$  or  $-N-$ ; and

(c) other than in the specific case in which  $Z_1$  represents  $-\text{CH}=\text{CH}-$ , and  $Z_2$  represents  $-\text{CH}-$ , when one  $Z_1$  and  $Z_2$  represents  $-\text{CH}-$ , then the other represents  $-\text{O}-$  or  $-\text{S}-$ ;

$R^4$  represents  $-\text{S}(\text{O})_2\text{N}(\text{H})\text{C}(\text{O})\text{R}^6$ ,  $-\text{S}(\text{O})_2\text{N}(\text{H})\text{S}(\text{O})_2\text{R}^6$ ,  $-\text{C}(\text{O})\text{N}(\text{H})\text{S}(\text{O})_2\text{R}^6$ ,  
 5 or, when  $Z_1$  represents  $-\text{CH}=\text{CH}-$ ,  $R^4$  may represent  $-\text{N}(\text{H})\text{S}(\text{O})_2\text{N}(\text{H})\text{C}(\text{O})\text{R}^7$  or  $-\text{N}(\text{H})\text{C}(\text{O})\text{N}(\text{H})\text{S}(\text{O})_2\text{R}^7$ ;

$R^5$  represents  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{C}_{1-6}$  alkoxy- $\text{C}_{1-6}$ -alkyl or di- $\text{C}_{1-3}$ -alkylamino- $\text{C}_{1-4}$ -alkyl;

$R^6$  represents  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{C}_{1-6}$  alkoxy- $\text{C}_{1-6}$ -alkyl,  
 10  $\text{C}_{1-3}$  alkoxy- $\text{C}_{1-6}$ -alkoxy,  $\text{C}_{1-6}$  alkylamino or di- $\text{C}_{1-6}$  alkylamino; and

$R^7$  represents  $\text{C}_{1-6}$  alkyl,

or a pharmaceutically-acceptable salt thereof.

2. A compound as claimed in Claim 1 wherein, when  $X_1$  represents  
 15  $-\text{C}(\text{R}^1)-$ , then  $X_3$  represents  $-\text{C}(\text{R}^2)-$  and  $X_4$  represents  $-\text{N}-$ .

3. A compound as claimed in Claim 2 wherein  $\text{R}^1$  represents H.

4. A compound as claimed in Claim 1 wherein, when  $X_1$  represents  
 20  $-\text{C}(\text{R}^1)-$ , then  $X_3$  and  $X_4$  both represent N.

5. A compound as claimed in Claim 1 wherein, when  $X_1$  represents  
 $-\text{C}(\text{R}^1)-$ , then  $X_3$  represents  $-\text{C}(\text{R}^2)-$  and  $X_4$  represents  $-\text{C}(\text{R}^3)-$ .

25 6. A compound as claimed in Claim 1, wherein, when  $X_1$  represents  
 $-\text{N}-$ , then  $X_3$  represents  $-\text{N}-$ .

7. A compound as claimed in Claim 6 wherein, when  $X_4$  represents  
 $-\text{C}(\text{R}^3)-$ , then  $\text{R}^3$  represents H.

8. A compound as claimed in Claim 1, wherein, when  $X_1$  represents  $-N-$ , then  $X_3$  represents  $-C(R^2)-$  and  $X_4$  represents  $-C(R^3)-$ .
9. A compound as claimed in Claim 1, wherein  $R^1$  represents H,  $C_{1-3}$  alkyl or  $CF_3$ .
10. A compound as claimed in Claim 9, wherein  $R^1$  represent H or ethyl.
11. A compound as claimed in Claim 1 wherein  $R^2$  represents  $C_{1-3}$  alkyl, halo or H.
12. A compound as claimed in Claim 11 wherein  $R^2$  represents H or methyl.
13. A compound as claimed in Claim 11 wherein  $R^2$  represents H.
14. A compound as claimed in Claim 1 wherein  $R^3$  represents  $C_{1-3}$  alkyl, halo or H.
15. A compound as claimed in Claim 14 wherein  $R^3$  represents H.
16. A compound as claimed in Claim 1 wherein  $Y_1$ ,  $Y_2$ ,  $Y_3$  and  $Y_4$  all represent  $-CH-$ .
17. A compound as claimed in Claim 1 wherein  $Z_1$  represents  $-S-$  or  $-CH=CH-$ .
18. A compound as claimed in Claim 17 wherein  $Z_1$  represents  $-S-$ .
19. A compound as claimed in Claim 1 wherein  $Z_2$  represents  $-CH-$ .

20. A compound as claimed in Claim 1 wherein  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$ .
- 5 21. A compound as claimed in Claim 1 wherein  $R^5$  represents *n*-butyl or *iso*-butyl.
22. A compound as claimed in Claim 21 wherein  $R^5$  represents *iso*-butyl.
- 10 23. A compound as claimed in Claim 1 wherein, when  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$ ,  $-S(O)_2N(H)S(O)_2R^6$  or  $-C(O)N(H)S(O)_2R^6$ ,  $R^6$  represents *n*-butoxymethyl, *iso*-butoxy or *n*-butoxy.
24. A compound as claimed in Claim 23 wherein  $R^6$  represents *n*-butoxy.
- 15 25. A compound as claimed in Claim 1 wherein, when  $X_1$ ,  $X_3$  and  $X_4$  all represent  $-CH-$ ,  $Y_1$ ,  $Y_2$ ,  $Y_3$  and  $Y_4$  all represent  $-CH-$ ,  $Z_1$  represents  $-S-$  or  $-CH=CH-$ ,  $Z_2$  represents  $-CH-$  and  $R^5$  represents *n*-butyl or *iso*-butyl, then  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$ , in which  $R^6$  represents  $-O$ -*n*-butyl,  $-O$ -*iso*-propyl,  $-O$ -*iso*-butyl or  $-CH_2$ - $O$ -*n*-butyl.
- 20 26. A compound as claimed in Claim 1, which is:  
*N*-butyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;  
 25 *N*-*iso*-butyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;  
*N*-*iso*-propyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;  
*N*-(butoxyacetyl)-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;  
 30

- N*-butyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-butylthiophene-2-sulfonamide;
- N*-butyloxycarbonyl-2-(4-imidazol-1-ylmethylphenyl)-4-*iso*-butylbenzene-sulfonamide;
- 5 *N*-butyloxycarbonyl-5-*iso*-butyl-3-(4-tetrazol-2-ylmethylphenyl)thiophene-2-sulfonamide;
- N*-butyloxycarbonyl-5-*iso*-butyl-3-(4-tetrazol-1-ylmethylphenyl)thiophene-2-sulfonamide;
- N*-butyloxycarbonyl-3-(4-[1,2,4]triazol-1-ylmethylphenyl)-5-*iso*-butyl-
- 10 thiophene-2-sulfonamide;
- N*-(butylamino)carbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;
- N*-butylsulfonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;
- 15 *N*-butylsulfonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-carboxamide;
- N*-butyloxycarbonyl-4-butyl-2-(4-imidazol-1-ylmethylphenyl)benzene-sulfonamide;
- N*-(2-methoxyethyloxy)carbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-
- 20 butylthiophene-2-sulfonamide;
- N*-ethyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;
- N*-*tert*-butyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;
- 25 *N*-butyloxycarbonyl-3-[4-(4-methylimidazol-1-ylmethyl)phenyl]-5-*iso*-butylthiophene-2-sulfonamide;
- N*-butyloxycarbonyl-3-(4-pyrazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide;
- N*-butyloxycarbonyl-3-[4-(3-trifluoromethylpyrazol-1-ylmethyl)phenyl]-5-
- 30 *iso*-butylthiophene-2-sulfonamide;

*N*-(*N*-butyl-*N*-methylamino)carbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-*iso*-butylthiophene-2-sulfonamide; or  
*N*-butyloxycarbonyl-3-(4-imidazol-1-ylmethylphenyl)-5-(2-methoxyethyl)-thiophene-2-sulfonamide.

5

27. A pharmaceutical formulation including a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

10

28. A method of treatment of a condition in which selective agonism of the AT<sub>2</sub> receptor is desired and/or required, which method comprises administration of a therapeutically effective amount of a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

15

29. The method as claimed in Claim 28, wherein the condition is of the gastrointestinal tract, the cardiovascular system, the respiratory tract, the kidneys, the eyes, the female reproductive (ovulation) system, or the central nervous system.

20

30. The method as claimed in Claim 28, wherein the condition is oesophagitis, Barrett's oesophagus, a gastric ulcer, a duodenal ulcer, dyspepsia (including non-ulcer dyspepsia), gastro-oesophageal reflux, irritable bowel syndrome, inflammatory bowel disease, pancreatitis, hepatic disorders (including hepatitis), gall bladder disease, multiple organ failure, sepsis, xerostomia, gastritis, gastroparesis, hyperacidity, a disorder of the biliary tract, coeliacia, Crohn's disease, ulcerative colitis, diarrhoea, constipation, colic, dysphagia, vomiting, nausea, indigestion, Sjögren's syndrome, inflammatory disorders, asthma, an obstructive lung disease (including chronic obstructive lung disease), pneumonitis, pulmonary

30

hypertension, adult respiratory distress syndrome, renal failure, nephritis, renal hypertension, diabetic retinopathy, premature retinopathy, retinal microvascularisation, ovulatory dysfunction, hypertension, cardiac hypertrophy, cardiac failure, arteriosclerosis, arterial thrombosis, venous thrombosis, endothelial dysfunction, endothelial lesions, post balloon dilatation stenosis, angiogenesis, diabetic complications, microvascular dysfunction, angina, cardiac arrhythmias, claudicatio intermittens, preeclampsia, myocardial infarction, reinfarction, ischaemic lesions, erectile dysfunction, neointima proliferation, cognitive dysfunctions, dysfunctions of food intake (hunger/satiety), thirst, stroke, cerebral bleeding, cerebral embolus, cerebral infarction, hypertrophic disorders, prostate hyperplasia, autoimmune disorders, psoriasis, obesity, neuronal regeneration, an ulcer, adipose tissue hyperplasia, stem cell differentiation and proliferation, cancer, apoptosis, tumours, hypertrophy diabetes, neuronal lesions or organ rejection.

31. The method as claimed in Claim 28, wherein the condition is non-ulcer dyspepsia, irritable bowel syndrome, multiple organ failure, hypertension or cardiac failure.

32. A pharmaceutical formulation including a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof, and an AT1 receptor antagonist, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

33. A kit of parts comprising components:

- (a) a pharmaceutical formulation including a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier; and

- (b) a pharmaceutical formulation including an AT1 receptor antagonist, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier,

which components (a) and (b) are each provided in a form that is suitable  
5 for administration in conjunction with the other.

34. A pharmaceutical formulation including a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof, and an angiotensin converting enzyme inhibitor, in admixture with a pharmaceutically-  
10 acceptable adjuvant, diluent or carrier.

35. A kit of parts comprising components:

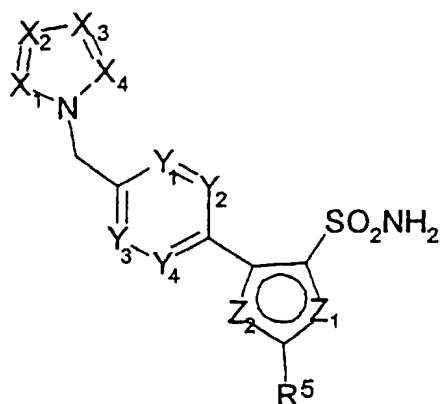
- (a) a pharmaceutical formulation including a compound as defined in Claim 1, or a pharmaceutically acceptable salt thereof, in admixture  
15 with a pharmaceutically-acceptable adjuvant, diluent or carrier; and  
(b) a pharmaceutical formulation including an angiotensin converting enzyme inhibitor, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier,

which components (a) and (b) are each provided in a form that is suitable  
20 for administration in conjunction with the other.

36. A process for the preparation of a compound as defined in Claim 1, which comprises:

- (i) for compounds of formula I in which  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$  or  $-S(O)_2N(H)S(O)_2R^6$ , and  $R^6$  is as defined in Claim 1, reaction of a  
25 compound of formula II,





II

wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ ,  $Y_1$ ,  $Y_2$ ,  $Y_3$ ,  $Y_4$ ,  $Z_1$ ,  $Z_2$  and  $R^5$  are as defined in Claim 1 with a compound of formula III,



III

5 wherein G represents  $C(O)$  or  $S(O)_2$  (as appropriate),  $L^1$  represents a suitable leaving group and  $R^6$  is as defined in Claim 1;

(ii) for compounds of formula I in which  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$  and  $R^6$  represents  $C_{1-6}$  alkoxy- $C_{1-6}$ -alkyl, coupling of a compound of formula II as defined above with a compound of formula IV,

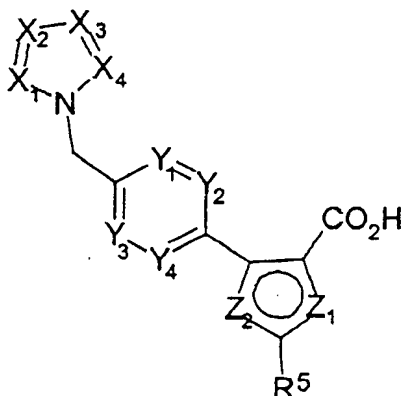
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IV

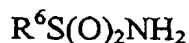
wherein  $R^{6a}$  represents  $C_{1-6}$  alkoxy- $C_{1-6}$ -alkyl;

(iii) for compounds of formula I in which  $R^4$  represents  $-C(O)N(H)S(O)_2R^6$  and  $R^6$  is as defined in Claim 1, coupling of a compound of formula V,



V

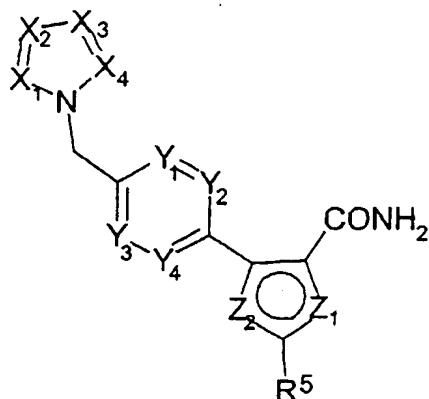
15 wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ ,  $Y_1$ ,  $Y_2$ ,  $Y_3$ ,  $Y_4$ ,  $Z_1$ ,  $Z_2$  and  $R^5$  are as defined in Claim 1, with a compound of formula VI,



VI

wherein  $R^6$  is as defined in Claim 1;

(iv) for compounds of formula I in which  $R^4$  represents  $-C(O)N(H)S(O)_2R^6$  and  $R^6$  is as defined in Claim 1, coupling of a compound of formula VII,



VII

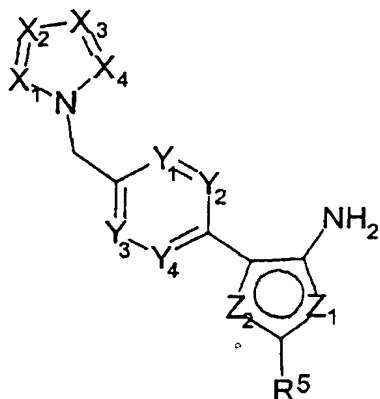
5 wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ ,  $Y_1$ ,  $Y_2$ ,  $Y_3$ ,  $Y_4$ ,  $Z_1$ ,  $Z_2$  and  $R^5$  are as defined in Claim 1, with a compound of formula VIII,



VIII

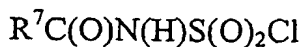
wherein  $R^6$  is as defined in Claim 1;

(v) for compounds of formula I in which  $R^4$  represents  
 10  $-N(H)S(O)_2N(H)C(O)R^7$  and  $R^7$  is as defined in Claim 1, reaction of a compound of formula IX,



IX

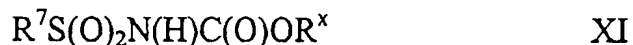
wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ ,  $Y_1$ ,  $Y_2$ ,  $Y_3$ ,  $Y_4$ ,  $Z_1$ ,  $Z_2$  and  $R^5$  are as defined in Claim 1, with a compound of formula X,



X

15 wherein  $R^7$  is as defined in Claim 1;

- (vi) for compounds of formula I in which  $R^4$  represents  $-N(H)C(O)N(H)S(O)_2R^7$  and  $R^7$  is as defined in Claim 1, reaction of a compound of formula IX as defined above with a compound of formula XI,



- 5 wherein  $R^x$  represents  $C_{1-2}$  alkyl and  $R^7$  is as defined in Claim 1;

- (vii) for compounds of formula I in which  $R^4$  represents  $-N(H)C(O)N(H)S(O)_2R^7$  and  $R^7$  is as defined in Claim 1, reaction of a compound of formula IX as defined above with a compound of formula XII,



- 10 wherein  $R^7$  is as defined in Claim 1;

- (viii) for compounds of formula I in which  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$  and  $R^6$  represents  $C_{1-6}$  alkylamino, reaction of a compound of formula II as defined above with a compound of formula XIII,



- 15 wherein  $R^{6b}$  represents  $C_{1-6}$  alkyl; or

- (ix) for compounds of formula I in which  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$  and  $R^6$  represents di- $C_{1-6}$  alkylamino, reaction of a corresponding compound of formula I in which  $R^4$  represents  $-S(O)_2N(H)C(O)R^6$  and  $R^6$  represents  $C_{1-6}$  alkoxy with a compound formula  
20 XIV,



wherein  $R^{6c}$  and  $R^{6d}$  independently represent  $C_{1-6}$  alkyl.

37. A compound of formula II as defined in Claim 36 or a protected  
25 derivative thereof.

38. A compound of formula II as claimed in Claim 36, or a protected derivative thereof, wherein  $X_1$ ,  $X_3$  and  $X_4$  all represent  $-CH-$ ,  $Y_1$ ,  $Y_2$ ,  $Y_3$  and  $Y_4$  all represent  $-CH-$ ,  $Z_1$  represents  $-S-$  or  $-CH=CH-$ ,  $Z_2$  represents  $-CH-$   
30 and  $R^5$  represents *n*-butyl or *iso*-butyl.

39. A compound of formula V as defined in Claim 36 or a protected derivative thereof.

5 40. A compound of formula VII as defined in Claim 36 or a protected derivative thereof.

41. A compound of formula IX as defined in Claim 36 or a protected derivative thereof.